Atrial Fibrillation and Atrial Flutter in Pregnant Women With Heart Disease
Contributions From the ROPAC Investigators*

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Atrial fibrillation (AF) and atrial flutter (AFL) are common supraventricular arrhythmias whose prevalence is associated with advanced age and comorbid conditions such as structural heart disease or hypertension. They are, however, uncommon arrhythmias in women of childbearing age. Although AF and AFL can occur in young women with structurally normal hearts, they often occur in the setting of structural heart disease. For those women who become pregnant, the hemodynamic and hormonal changes can aggravate the arrhythmias, and the prothrombotic state of pregnancy can contribute to thromboembolic complications. Management of AF and AFL is more complex during pregnancy because of the effects of medications on the developing fetus. Unfortunately, there are limited data on pregnancy risk and management strategies in this population.

In this issue of JACC: Clinical Electrophysiology, the multinational ROPAC (Registry on Pregnancy and Cardiac Disease) investigators report on the clinical presentation and management of AF/AFL in a large cohort of women with heart disease (1). Of the 1,321 women in the registry, 1.3% (n = 17) had AF/AFL during pregnancy. Although the overall incidence of AF/AFL in pregnant women with heart disease was relatively rare, women with mitral valve disease were at higher risk (2.5%) compared with women with other cardiac lesions. Atrial arrhythmias in women with mitral valve disease have been previously reported (2-4). Although some cases of AF/AFL occurred in women with congenital heart disease (i.e., ventricular septal defects, atrioventricular septal defects, Fontan circulation), overall, in women with congenital lesions, AF/AFL rarely developed (0.7%).

The increased maternal mortality (12% of pregnancies complicated by AF/AFL) seen in this study highlights the association between atrial arrhythmias and serious outcomes in pregnant women with structural heart disease. Although mortality in women with rheumatic mitral valve disease is rare in developed countries (2,3), mortality as high as 32% has been reported in women with rheumatic heart disease in sub-Saharan Africa (4). The maternal mortality in this study underscores the need for appropriate preconception counseling, pre-pregnancy interventions when appropriate, frequent surveillance during pregnancy, and the need for pregnancy care by a multidisciplinary team with expertise in pregnancy and heart disease.

The ROPAC study reports on symptomatic arrhythmias (5); however, some arrhythmias are not clinically apparent and are only detected by continuous rhythm monitoring. Rhythm monitoring is suggested for patients with symptoms attributable to arrhythmias, but monitoring in asymptomatic patients is not typically recommended. In view of the increased pregnancy mortality, perhaps routine pregnancy monitoring should be considered for all pregnant women with structural heart disease at high risk of atrial arrhythmias.

Beta-blockers were the most commonly used medication for the treatment of AF/AFL in the current study. Apart from arrhythmia therapy, beta-blockers...
offer additional advantages to women with conditions such as mitral stenosis by slowing the heart rate, allowing for longer diastolic filling time and improved maternal hemodynamics. Beta-blockers are considered class C by the U.S. Food and Drug Administration (FDA). Their use during pregnancy has been associated with low birth weight, fetal bradycardia, and neonatal hypoglycemia (6); however, maternal benefits may outweigh potential fetal/neonatal risks. The risks and benefits of any medication must be discussed with the patient before initiation of therapy. At our site, we commonly use metoprolol for to treat atrial arrhythmias during pregnancy. Metoprolol is more effective in reducing the ventricular rate in AF/AFL than labetalol (7). Metoprolol can also be used while breastfeeding (6,8). Atenolol is an FDA class D medication and is often avoided because of its association with low birth weight. Calcium channel blockers can also be used to treat atrial arrhythmias. Although not used in women in this study, oral verapamil is an FDA class C medication and can be effective in tachycardia management. Intravenous verapamil is often avoided because of the potential for maternal and neonatal hypotension. There are concerns related to teratogenicity with the use of diltiazem in animal studies at high doses, and therefore it is typically avoided in pregnancy when other options are available (9). Digoxin is most often used in combination with other agents to control ventricular rate and is most effective at controlling ventricular response at rest (7,10). Digoxin, an FDA class C medication, has a long history of use in pregnancy (9) and has been used for the management of fetal arrhythmias (11). Orally administered digoxin is excreted into breast milk at very low concentrations and is considered to be safe for use during lactation (12). Although other antiarrhythmic drugs can be used to treat AF/AFL in women with heart disease, they are associated with potential serious adverse side effects, particularly the risk of proarrhythmia. The use of these antiarrhythmic medications needs to be individualized. Outside of pregnancy, amiodarone and sotalol are recommended for the treatment of atrial arrhythmias in patients with structural heart disease (13). Sotalol is an FDA class B medication and can be used to restore and maintain sinus rhythm, but therapy may be limited by fetal bradycardia (14). Sotalol results in maternal QT interval prolongation and potentially life-threatening arrhythmias and should only be used with close maternal monitoring (15). Amiodarone is contraindicated during pregnancy because of its effect on the fetal thyroid function, but may be necessary in some patients with complex structural heart disease in whom other antiarrhythmic agents are ineffective or contra-indicated (6,16). Amiodarone was used during pregnancy in 2 women with AF/AFL in this study. Flecainide has been used to treat fetal arrhythmias, but fewer data are available on its safety for the treatment of maternal arrhythmias (17). It is often avoided in women with structural heart disease (18).

For women presenting with new AF/AFL, cardioversion is often the treatment strategy of choice because rhythm control is preferred over rate control. Before electrical or chemical cardioversion, it is important to consider precipitating factors and the need for pre-cardioversion anticoagulation. When required, cardioversion can be performed during pregnancy. For recurrent arrhythmias or those that result in significant maternal decompensation, treatment with catheter ablation can be an option. Even a “minimal” x-ray approach, with shielding of the mother and fetus, cannot fully eliminate radiation exposure. There is growing experience with ablation not requiring fluoroscopic exposure (19).

Both AF/AFL and pregnancy predispose to thromboembolic complications. In this study, 1 woman with AF/AFL and mitral valve disease died postpartum due to a presumed thromboembolic event. There were no other thromboembolic complications. All women in this series were treated with anticoagulants (low molecular weight heparin or vitamin K antagonists). Anticoagulation of the pregnant patient is more complex than of the nonpregnant patient. There are increased risks of spontaneous miscarriage, fetal deaths, and bleeding at the time of delivery in women using anticoagulants. Warfarin is teratogenic and is often avoided during organogenesis (between 6 and 12 weeks’ gestation). Heparin does not cross the placenta and is a safe alternative to warfarin during pregnancy and, in this series, was the most commonly used an anticoagulant. Because of better bioavailability, low molecular weight heparin is preferred over unfractionated heparin at many centers. However, dosing of low molecular weight heparin requires adjustment during pregnancy and anti-Xa levels need to be checked. The safety of direct oral anticoagulants during pregnancy is not established, and animal data suggest potential harm with dabigatran (20). Women taking warfarin must be transitioned to heparin before delivery to prevent maternal and neonatal bleeding. Management of anticoagulation at the time delivery is complex, and delivery must be carefully coordinated by the health care team.

In addition to maternal morbidity and mortality, the rates of fetal and neonatal complications in this study were also concerning (1). Low birth weight was more common in women with AF/AFL. There was also
a trend for higher rates of intrauterine growth retardation and premature births in women with AF/AFL. High rates of fetal and neonatal complications in women with structural heart disease in whom arrhythmias develop have been reported by other groups (3,21). The mechanisms by which these fetal and neonatal complications develop are not understood but may be related to factors such as abnormal maternal hemodynamics or medication side effects and require further study.

Multicenter collaborative studies, such as the ROPAC, continue to help improve our understanding of pregnancy risk in women with rare conditions and rare complications.

REFERENCES


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